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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,782	08/08/2006	Sang Yup Lee	4240-148	8819

23448 7590 03/19/2010

INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER	
VOGEL, NANCY TREPTOW	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
03/19/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,782	LEE ET AL.	
	Examiner	Art Unit	
	NANCY VOGEL	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/4/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4-13 are pending in the claims.

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are no new grounds of rejection that were not necessitated by applicants' amendment and therefore, this action is final.

The following rejections are maintained essentially for the reasons made of record in the previous Office action, mailed 3/4/09. To recapitulate:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 11, 12, are rejected under 35 U.S.C. 103(a) as being unpatentable over Francisco et al. (Proc. Natl. Acad. Sci USA 90 10444-10448, 1993), or Charbit et al. (Gene 70, 1, 181-189, 1988) in view of Lee et al. (Trends in Biotechnol., 21, 1, 45-52) and Cristalli et al. (Arch. Biochem. Biophys., 377, 2, 324-333, 2000) (all but Lee et al. cited by applicants).

Francisco et al. and Charbit et al. each disclose a vector for expressing a target protein on the surface of cells, comprising a gene encoding a surface display outer

membrane protein, and antibiotic-resistant gene, a promoter, and a gene encoding a target protein in which the target protein is expressed on the surface of the cell in a form fused with the surface display outer membrane protein. (See page 10444, right col., third paragraph, and page 1045-1046, Francisco et al; see abstract, pages 181-185 of Charbit et al.). The different between the references and the instant claims is that the surface display outer membrane is the fadL protein. However, Cristalli et al. disclose the outer member protein FadL and its structure, including externally exposed domains (see abstract, see page 330). Lee et al. disclose the general method of displaying proteins of choice on the surface of microbes using fusions such as C-terminal, N-terminal, or sandwich type fusions of the protein of choice with "carrier proteins", which are outer membrane proteins (see abstract, see page 45-49). It would have been obvious to one of ordinary skill in the art to have utilized the known outer membrane protein FadL in the method disclosed by Francisco et al. and Charbit et al., and further generally disclosed in Lee et al., since the structure of the FadL protein, including proposed regions which are displayed on the surface were known, and since the references all are concerned with surface display type proteins. One would have been motivated to do so by the teachings of Lee et al. , which disclose generally that a protein that is located on the outer membrane surface of a microbe may be used as an anchor protein for surface display, and by Cristalli et al. which particularly disclose the outer membrane protein FadL and its surface topology, making it a good candidate for surface display. Based upon the teachings of the cited references, the high skill of one

of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1-7, 11, 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Francisco et al. (Proc. Natl. Acad. Sci USA 90 10444-10448, 1993), or Charbit et al. (Gene 70, 1, 181-189, 1988) in view of Lee et al. (Trends in Biotechnol., 21, 1, 45-52) and Cristalli et al. (Arch. Biochem. Biophys., 377, 2, 324-333, 2000) (cited by applicants) as applied to claim 1-5, 7, 11 and 12 above, and further in view of Park et al. (FEMS Micrbiol. Lett. 214, 217, 2002) or DeBoer et al. (Proc. Nat. Acad. Sci USA 80, 21-25, 1983).

Francisco, Charbit, Lee and Cristalli are cited essentially for the reasons set forth above. The difference between the references and the instant claims is that particular promoters, i.e. Tac or gntT104 promoters, are used. However, each of these promoters are known in the art as disclosed by Park et al. and DeBoer et al. (see abstract of both). In addition, Charbit discloses the pTac promoter for the expression of the heterologous protein (see page 182). It would have been obvious to have utilized these known promoters for their known useful properties of controlling high levels of production of a protein of interest, in which the gene encoding said protein of interest is operatively linked to the promoter. One would have been motivated to do so by the ability of each of these promoters to control expression in either a constitutive or inducible manner. The substitution of one promoter for another, for the intended purpose of using the promoter for known properties, would have been obvious to one of ordinary skill in the

art. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1-5, 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Francisco et al. (Proc. Natl. Acad. Sci USA 90 10444-10448, 1993), or Charbit et al. (Gene 70, 1, 181-189, 1988) in view of Lee et al. (Trends in Biotechnol., 21, 1, 45-52) and Cristalli et al. (Arch. Biochem. Biophys., 377, 2, 324-333, 2000) (cited by applicants) as applied to claim 1-5, 7, 11 and 12 above, and further in view of Georgiou et al. (US Patent 5,508, 192).

Francisco et la., Charbit, Lee, Cristalli are cited essentially for the reasons set forth above. The difference between the references and the instant claims is that protease deficient host microorganisms, particularly E. coli, are used to facilitate the cell surface expression of the target protein. However, Georgiou et al. teaches transformed E. coli having mutations in proteases such as degP, ompT, ptr, or prc, and further teaches the motivation to utilize such strains in order to prevent the degradation of recombinant proteins produced in the cell (see col. 1-4). It would have been obvious to have used such strains in order to prevent degradation of the recombinantly produced protein of interest, as is taught in the reference. One would have been motivated to do so by the desire to produce non-degraded recombinant proteins on the surface of the cell. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the

art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1-5, 7, 11, 12, 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Francisco et al. (Proc. Natl. Acad. Sci USA 90 10444-10448, 1993), or Charbit et al. (Gene 70, 1, 181-189, 1988) in view of Lee et al. (Trends in Biotechnol., 21, 1, 45-52) and Cristalli et al. (Arch. Biochem. Biophys., 377, 2, 324-333, 2000) (cited by applicants) as applied to claims 1-5, 7, 11, 12 above, and further in view of Pan et al. (US Patent 6,071,725).

Francisco, Charbit, Lee, and Cristalli are cited essentially for the reasons set forth above. The difference between the references and the instant claims is that the foreign gene that is expressed is a lipase gene. However, Pan et al. disclose a method of recombinant production of a lipase on the cell surface using a surface display protein in a recombinant microorganism (see col. 4-5). It would have been obvious to have expressed lipase in the method disclosed by the Francisco Charbit, Lee and Cristalli references, since such a method was known to be useful for the surface of a protein of choice, and since Pan et al. disclosed that lipase may be expressed using a method of surface display of a target protein by fusion with a surface protein in a microorganism. One would have been motivated to do so by the desire to express a lipase protein on the surface of a microorganism, as taught by the reference. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicant's arguments are directed towards all of the above rejections. Applicant's arguments have been considered but have not been found convincing. Applicants have argued that there was not expectation of success in using the fadL gene for surface display of proteins in recombinant microorganisms. Applicants have argued that none of the cited references provide any demonstration that all outer membranes are readily functional as a surface anchoring motif, and further argue that other references (Lee et al. 2005) show that various fusion positions were found to be unsuitable for larger protein display. However, the fact that the references cited disclose at least 5 widely diverse outer membrane proteins that are used as surface anchoring motifs (page 7) shows that any outer membrane protein, such as fadL, is likely to be a useful outer display protein. There is no reasons cited to expect that fadL would differ from the known outer display proteins. Therefore, the rejections are maintained.

The following rejection is necessitated by applicant's amendment:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and by dependence claims 5-13 are vague and indefinite in the recitation of "the C-terminal end of the fadL gene is truncated at a truncation point", since it is not clear what is intended by this phrase. It is not clear whether it is intended that the complete fadL gene is never present, i.e. the gene must be incomplete, or whether the complete gene could be present and the "truncation point" could be after the complete gene. Therefore the intended metes and bounds of the claimed subject matter cannot be determined.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
3/15/10